

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently Amended) A purified functional polynucleotide comprising a tripartite construct having three functional domains, said functional domains comprising ¶
(a) an actuator domain comprising at least a fragment of a pre-existing actuator nucleotide sequence, ¶
(b) a receptor domain comprising at least a fragment of a pre-existing receptor nucleotide sequence, and ¶
(c) a randomized bridging domain comprising a random nucleotide sequence a communication module, wherein said communication module is a generic reporter of an occupation state of said receptor domain, ¶
and wherein interaction of the receptor domain with a signaling agent triggers a conformational change in the randomized bridging domain which modulates the activity of the actuator domain.
2. (Previously Amended) A polynucleotide according to claim 1 wherein the signaling agent is a ligand that binds to the receptor domain.
3. (Original) A polynucleotide according to claim 1 wherein the activity of the actuator domain is catalytic.
4. (Original) A polynucleotide according to claim 1 wherein at least two of the domains are non-overlapping.
5. (Original) A polynucleotide according to claim 1 wherein at least two of the domains are partially or completely overlapping.
6. (Original) A polynucleotide according to claim 1 which is RNA.

7. (Original) A polynucleotide according to claim 6 which is a hammerhead ribozyme.
8. (Cancelled)
9. (Original) A polynucleotide according to claim 1 wherein the actuator domain exhibits catalytic activity that is triggered by binding of a chemical compound to the receptor domain.
10. (Previously Amended) A biosensor comprising a polynucleotide according to claim 1.
11. (Original) A biosensor according to claim 10 in which the polynucleotide is attached to a solid support.
12. (Previously Amended) A method for detecting the presence or absence of a ligand or its concentration in a sample comprising contacting the sample with a polynucleotide according to claim 1.
13. (Original) A method according to claim 12 wherein the presence or absence of a ligand or its concentration is determined by observation of a chemical reaction.
14. (Original) A method according to claim 12 wherein the presence or absence of a ligand or its concentration is detected by observation of a change in polynucleotide configuration or function.
15. (Currently Amended) A process for preparing polynucleotides that are responsive to the presence or absence of a signaling agent, comprising linking together three functional domains comprising a polynucleotide actuator domain ~~comprising at least a fragment of a pre-existing actuator nucleotide sequence~~, a receptor domain ~~comprising at least a fragment of a pre-existing receptor nucleotide sequence~~, and a ~~randomized~~ bridging domain comprising ~~a random nucleotide sequence~~ a communication module, wherein said communication module is a generic reporter of an occupation state of said receptor domain, such that interaction of the signaling

agent with the receptor domain triggers a conformational change in the randomized bridging domain which modulates the activity of the actuator domain.

16. (Original) A process according to claim 15 wherein the receptor domain has a ligand binding site and wherein ligand binding triggers a conformational change in the bridging domain that stimulates catalytic activity of the actuator domain.

17. (Currently Amended) A process of identifying a generic bridging domain that modulates the activity of two or more different actuator domains, for screening polynucleotides which have an actuator domain, a receptor domain, and a randomized bridging domain and which are responsive to a signaling agent in a sample, comprising:

(a) preparing a pool of polynucleotides, wherein each polynucleotide in said pool comprises a first actuator domain having a pre-existing actuator domain nucleotide sequence and a receptor domain having a pre-existing receptor nucleotide sequence linked by linking a randomized bridging domain comprising a random nucleotide sequence, wherein the receptor domain is responsive to a first signaling agent; and having defined properties that modulate the activity of a corresponding actuator domain having defined properties and comprising at least a fragment of a pre-existing actuator nucleotide sequence, to a receptor domain having a random sequence, and

(b) incubating a sample containing the first signaling agent with the polynucleotide pool and identifying which polynucleotides in said pool are responsive to the presence of the first signaling agent by incubating the sample with the polynucleotide so constructed and by observing modulation of the activity of the actuator domain;

(c) determining the nucleotide sequence of the randomized bridging domain in each responsive polynucleotide identified in step (b), thereby identifying functional bridging domains that modulate the activity of the first actuator domain; and

(d) determining whether each functional bridging domain modulates the activity of at least a second actuator domain in the presence of at least one signaling agent that is different from the first signaling agent, thereby identifying generic bridging domains that modulate the activity of two or more different actuator domains.

18. (Currently Amended) A process according to claim 17 wherein the receptor domain has a ligand binding site and wherein ligand binding triggers a conformational change in the randomized bridging domain that stimulates catalytic activity of the first actuator domain.

19. (Previously Amended) A process for preparing RNA sensors according to claim 15.

20. (Cancelled)

21. (New) The process according to claim 17, wherein the generic bridging domains are identified by:

(i) preparing a second pool of polynucleotides, wherein each polynucleotide in said pool comprises a second actuator domain having a pre-existing actuator domain nucleotide sequence and a second receptor domain having a pre-existing receptor nucleotide sequence linked by a functional bridging domain selected from the bridging domains determined in step (c), wherein the second receptor domain is responsive to a second signaling agent;

(ii) incubating a second sample containing the second signaling agent with the second polynucleotide pool and identifying which polynucleotides in said second pool are responsive to the presence of the second signaling agent;

(iii) determining the nucleotide sequence of the functional bridging domain in each responsive polynucleotide identified in step (i), thereby identifying generic bridging domains, wherein the generic bridging domain of each polynucleotide responsive to the first and second signaling agents is a reporter of the occupation state of the first and second receptor domains; and

(iv) repeating steps (i), (ii) and (iii) for each functional bridging domain identified in step (c) to identify a pool of generic bridging domains.

22. (New) A method for identifying a functional bridging domain that modulates the activity of an actuator domain, comprising:

- (a) preparing a pool of polynucleotides, wherein each polynucleotide in said pool comprises an actuator domain having a pre-existing actuator domain nucleotide sequence and a receptor domain having a pre-existing receptor nucleotide sequence linked by a randomized bridging domain comprising a random nucleotide sequence, wherein the receptor domain is responsive to a signaling agent;
- (b) incubating a sample containing the signaling agent with the polynucleotide pool and identifying which polynucleotides in said pool are responsive to the presence of the signaling agent; and
- (c) determining the nucleotide sequence of the randomized bridging domain in each responsive polynucleotide identified in step (b), thereby identifying functional bridging domains that modulate the activity of the actuator domain.